REMARKS

Claims 1-9 and 15 have been amended to clearly point out and distinctly claim what Applicant regards as the subject matter of the present invention. Claims 1 and 6-8 have been amended to recite an effective amount in IU/kg. Support for these amendments may be found in Claim 1 as originally filed.

Claims 3-8 have been amended to provide proper antecedent basis for the language used in the claims and to clarify the dosing regimen. Support for these amendments may be found throughout the specification as filed. Specifically, for claims 3-5 support may be found at page 7, lines 1-6, and for Claims 6-8 support may be found in Claims 1 and 6-8 as originally filed.

Claim 9 has been amended to recite the co-administration of interferon with other cytokines or interferon inducers. Support for this amendment may be found at page 4, lines 10-13.

Claim 15 has been amended to clarify that the composition is provided in a unitary dosage form. Support for this amendment may be found at page 4, lines 6-9.

No new matter is introduced by these amendments and their entry is respectfully requested.

Objection to Claims 13 and 14 under 37 CFR §1.75(b)

Claims 13 and 14 stand objected to under 37 CFR §1.75(b) as allegedly being duplicate claims. Applicant respectfully disagrees. Claim 13 is drawn to a method that uses an interferon comprising a Type II interferon. Claim 14 further limits the Type II interferon to a gamma-interferon. The possibility that there may exist other Type II interferons or sub-classes of gamma-interferon should not be precluded. Thus, Applicant believes that claims 13 and 14 are in fact different in scope and content. Applicant respectfully requests that the objection be withdrawn.

Rejections Under 35 USC §112, second paragraph

Claims 1 and 3-14 stand rejected under 35 USC §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which is the invention. Claims 1, 3-5 and 9-14 are alleged to not be clear whether they are limited to the treatment of 70 kg humans or, alternatively, what amounts of IFN should be administered to subjects other than humans having a mass of 70 kg. Claim 1 has been amended to recite an effective amount in IU/kg. Claims 3-5 and 9-14 depend from claim 1 and, thus, incorporate the amendments clarifying the effective amount.

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Claims 3-8 are alleged to lack an unambiguous antecedent basis. The claims have been amended to provide the required antecedent basis.

Claims 4 and 5 have been amended to provide the antecedent basis and clarify the response against which the "smaller" doses must be compared. Additionally, claim 4 now recites that the lesser amounts, i.e., lower doses, distributed over time, so that the net effect is equivalent to the single administration of the effective amount.

Applicant submit that the amendments to the claims render the rejections moot and respectfully request their withdrawal.

Rejections under 35 USC §102(b)

In order to anticipate a prior art reference must contain within the four corners of the document all the functional and quantitative limitations of the claimed invention. The presently claimed invention is directed to the oromucosal administration of an interferon in an amount that provides effective treatment and/or prevention of disease without inducing a pathological response. It is a critical aspect, and one not found in the prior art, that no pathological response is induced by the oromucosal administration of the interferon at the doses claimed. Thus, in order to fully anticipate a prior art reference must contain the following elements for the method claims: 1) oromucosal interferon administration; 2) of a therapeutically effective amount; 3) without a pathological response; and 4) in dosages from about 21.4 IU/kg to about 2.9×10^4 IU/kg. In order to fully anticipate a prior art reference must contain the following elements for the composition claims: 1) a unit dosage form; 2) comprising a therapeutically effective amount from about 1500 IU to about 20×10^6 IU interferon; 3) for oromucosal administration; and 4) that does not induce a pathological response.

Claims 1, 2, 4, 5, 10, 11, and 15

Claims 1, 2, 4, 5, 10, 11, and 15 stand rejected under 35 USC §102(b) as being anticipated by Cummins (U.S. Patent 5, 019,382). Claims 1, 2 and 15 are independent claims; claims 4, 5, 10 and 11 are dependent claims and depend from claim 1. The Examiner alleges that Cummins meets all of the functional and quantitative limitations of the claims. Applicants respectfully disagree. Cummins teaches administering interferon at 0.7 IU/lb, which is clearly less than the 21.4IU/kg claimed in compositions comprising of 100 IU, which does not anticipate a composition having from about 1500 to 20×10^6 IU. Thus, the Cummins patent does not anticipate the instant claimed invention.

Claims 1-8, 10-12 and 15-18

Claims 1-8, 10-12 and 15-18 stand rejected under 35 USC §102(b) as being anticipated by Samo *et al.* Samo teaches the intranasal administration of either 0.7×10^6 or 2.4×10^6 units of interferon. As Applicant has explained in the specification (pg. 24-30), oromucosal administration requires more than just internasal delivery. Specifically, Applicants provide at page 11, lines 12-17:

> For the purposes of the animal experiments described in this specification, it will be clearly understood that the expression "intranasal/oral" or "intranasal plus oral" or "in/or" or "oromucosal" or "oropharyngeal" with reference to the route of administration of IFN is to be taken to mean administration of the IFN preparation deep into the nasal cavity so that it is rapidly distributed into the oropharyngeal cavity, i.e. **the mouth and throat of the recipient mammal**, so as to make contact with the mucosa lining this cavity. (Emphasis added.)

There is no teaching of oromuscosal delivery in Samo. Thus, Samo fails to meet this critical limitation of the claimed invention.

Samo also fails to meet other critical claim limitations, namely the limitation that no pathological reaction be induced. As noted in the reference at page 186, second column, 15% of the volunteers receiving 2.4×10^6 units interferon had to discontinue treatment due to side effects, i.e., blood mixed with mucus and superficial mucosal erosions. Further, the lower dose (0.7×10^6 units) not only had a complication rate of 5.5% (see Table 2 at page 186), but also was ineffective. In contrast, the method of this invention is not only effective, but does not induce any pathological response, let alone a toxic response. Therefore, Samo additionally fails to meet this critical limitation of the claimed invention.

Further, Claim 2 is directed to a method of treatment of various conditions. As this rejection applies to Claim 2, Applicant notes that Samo's use of interferon is prophylactical only. Thus, there is no treatment of a condition; there is arguably the prevention of a condition, i.e., prophylactic use of interferon. This is shown at page 182 of the reference, the volunteers were inoculated with the virus 2 hours *after* the second dose of interferon. Thus, the volunteers were not being treated for any condition at the time of administration.

For the foregoing reasons, Samo fails to anticipate the claimed invention.

Claims 1-3, 5 and 13-15

Claims 1-3, 5 and 13-15 stand rejected under 35 USC §102(b) as being anticipated by Iida *et al.* For the reasons noted above for the rejection based on Samo, Iida also fails to anticipate the claimed invention because intranasal administration is not the same as oromucosal. Further, as applied to Claim 2, Iida fails to show any benefit if the interferon is administered after infection. As applied to claim 15, Iida fails to disclose a unit dose composition meeting the limitation of 1500 IU. Thus, for the foregoing reasons, Iida fails to anticipate the claimed invention.

Rejection under 35 USC §103(a)

Initially, Applicants note that the test for non-obviousness articulated by the Court of Appeals for the Federal Circuit requires that the combination of the teachings of all or any of the references would have suggested the possibility of further improvement by combining such teachings. Thus, both the suggestion and reasonable expectation of success must be founded in the prior art, not in the Applicant's disclosure. *See* In re Vaeck, 20 USPQ2d 1439 (Fed Cir. 1991).

Claim 9

Claim 9 stands rejected under 35 USC §103(a) as being unpatentable over Iida *et al.* Claim 9 depends from Claim 1 and further comprises the co-administration of other cytokines or interferon inducers. As stated above, Iida fails to disclose the use of interferon oromucosally in an amount claimed by Applicants. Further, Iida fails to provide any motivation for the co-administration of other cytokines or interferon inducers, or suggest that an improved response may be obtained by such a co-administration. Therefore, one skilled in the art would not be motivated to co-administer IFN with either other cytokines or interferon inducers via the oromucosal route. It is the prior art, and not the Applicant's disclosure, that must establish the obviousness of the combination. Thus, Iida fails to render obvious such a method as described by claim 9.

Claims 1-18

Claims 1-18 stand rejected under 35 USC §103(a) as being unpatentable over Cummins in view of either Samo *et al.* or Iida *et al.* The combination of Cummins and Iida *et al.*, or Cummins and Samo *et al.*, is not suggested by either reference. Cummins does not suggest any dose of interferon greater than 4 IU/lb (see Column 8, line 23) should be used. In fact, Cummins typically uses a dose of about 1

IU/lb or less. Although Iida uses a higher dose, given the known toxicity of interferon in the art, the skilled artisan would not be motivated to increase the dosage. Indeed, Samo *et al.* teaches away from increasing the dose by noting that an increased incidence of adverse side effects is seen with increasing dosages of interferon. See Table 2, at page 186, of the Samo reference. Thus, one skilled in the art would not be motivated to combine Cummins with either Samo or Iida to obtain the claimed invention. Applicant respectfully request that the rejection be withdrawn.

Conclusion

In view of the foregoing amendments and remarks, Applicants respectfully request reconsideration and allowance on the merits of all pending claims.

Respectfully submitted,

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